UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

ANTIMICROBIALS DIVISION (AD)

September 13, 2016

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 46781-RU
DP Barcode: D434676
Product Name: CaviWipes Bleach

From: Chris Jiang, Chemist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: for Karen Hicks, Team Leader
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To: Demson Fuller PM 34/Donna Kamarei
Regulatory Management Branch II
Antimicrobials Division (7510P)

Applicant: Metrex Research

FORMULATION FROM LABEL:

PC Code	Active Ingredient(s):	% by wt.
014703	Sodium hypochlorite	0.91
	Other Ingredient(s):	99.09
	Total:	100.00

BACKGROUND: Metrex Research has submitted a label, CSFs (Confidential Statements of Formula) for the basic formulation and alternate formulation 1, and a set of six acute toxicity studies for this non-integrated product end-use product. The studies include an acute oral toxicity study (MRID 49921705), an acute dermal toxicity study (MRID 49921706, an acute inhalation toxicity study (MRID 49921707), an eye irritation study (MRID 49921708), a dermal irritation study (MRID 49921709), and a skin sensitization study (MRID 49921710).

RECOMMENDATIONS:

1. The acute toxicity studies **are acceptable.**

2. The acute toxicity profile for File Symbol 46781-RU is currently.

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	49921705	IV	Acceptable
Acute Dermal Toxicity	49921706	IV	Acceptable
Acute Inhalation Toxicity	49921707	IV	Acceptable
Primary Eye Irritation	49921708	IV	Acceptable
Primary Dermal Irritation	49921709	IV	Acceptable
Dermal Sensitization	49921710	Nonsensitizer	Acceptable

LABELING

1 The optional signal word is **CAUTION.**

The policy on antimicrobial towelettes and wipes is under consideration by the Antimicrobial Division. Once the policy has been finalized, registrants will be informed if there are changes that need to be made regarding the registration process and if there are any additional data that must be submitted to the Division for review.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100)

Product Manager: Demson Fuller
MRID No.: 49921705

Reviewer: Chris Jiang
Study Completion Date: April 26, 2016
Study No.: 19754-16

Testing Laboratory: Stillmeadow, Inc.
Author: Lori Carter

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Dose level: 5000 mg/kg

Species: Female Sprague-Dawley rats
Age: Nine weeks
Weight: 184 to 196 grams on day 0
Source: Texas Animal Specialties, Humble, TX

Conclusions:

1. **LD_{50} (mg/kg):** $LD_{50} > 5000$ mg/kg
2. **The estimated LD_{50} is greater than 5000 mg/kg.**
3. **Toxicity Category:** IV **Classification:** Acceptable

Results:

Reported Mortality

Animal Number	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
51	5000	O	O
52	5000	O	O
53	5000	O	O

O = Survival; X = Death

Clinical signs:

5000 mg/kg: All animals were active and healthy through the study.

Gross necropsies:

5000 mg/kg: One female had lungs pale with dark spots and another female had pale mottled lungs.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200)

Product Manager: Demson Fuller
MRID No.: 49921706

Reviewer: Chris Jiang
Study Completion Date: April 26, 2016
Study No.: 19755-16

Testing Laboratory: Stillmeadow, Inc.
Author: Lori Carter

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Dose level: 5050 mg/kg

Species: Five male and five female Sprague-Dawley rats
Age: Eight weeks
Weight: ♂: 176 to 213 grams on day 0; ♀: 253 to 292 grams on day 0
Source: Texas Animal Specialties, Humble, TX

Conclusions:

1. **LD_{50} (mg/kg):** Males: LD_{50}> 5050 mg/kg
   Females: LD_{50}> 5050 mg/kg
   Combined: LD_{50}> 5050 mg/kg
2. **The estimated LD_{50} is greater than 5050 mg/kg for males and females.**
3. **Toxicity Category:** IV **Classification:** Acceptable

Deviations from guideline 870.1200: Temperature and relative humidity were at times outside the protocol range.

Reported Mortality

Dose Level (mg/kg)	Number Dead / Number Tested		
	Males	Females	Combined
5050	0 / 5	0 / 5	0 / 10

Clinical signs:

5050 mg/kg: All animals were active and healthy through the study.

Gross necropsies:

5050 mg/kg: Gross necropsies were unremarkable except for one female who had gas in the cecum.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING
(870.1300)

Product Manager: Demson Fuller
MRID No.: 49921707

Reviewer: Chris Jiang
Study Completion Date: April 29, 2016
Study Amended Date: May 11, 2016
Study No.: 19756-16

Testing Laboratory: Stillmeadow, Inc.
Author: Andrew Doig

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Gravimetric: 2.21 mg/L **Nominal:** 5.69 mg/L

Species: Five male and five female Sprague-Dawley rats
Age: Eight weeks
Weight: ♂: 235 to 280 grams on day 0; ♀: 170 to 182 grams on day 0
Source: Texas Animal Specialties, Humble, TX

Summary:

1. **LC_{50} (mg/kg):** LC_{50} > 2.21 mg/L
2. **The estimated LC_{50} is greater than 2.21 mg/L.**
3. **MMAD:** 2.6 µm
4. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviations from 81-3): Two female weights were under protocol range and relative humidity was at times outside protocol range. These deviations did not impact the integrity of the study.

Results:

Reported Mortality

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2.21 mg/L	0/5	0/5	0/10

Chamber Atmosphere			
Dose Level	MMAD (µm)	GSD (µm)	% particles < 3.2 µm
2.21 mg/L	2.6	1.8	50.00
2.21 mg/L	2.5	2.0	20.00

Chamber Environment	
Chamber Volume (L)	500 Liters
Airflow (LPM)	385 LPM
Temperature (°C)	23.3 to 24.1
Relative Humidity (%)	74 to 88

Clinical Observations: All animals were active and healthy through the study.

Gross Necropsy Findings: Three males had pale lungs and four females had pale lungs.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (81-4, 870.2400)

Product Manager: Demson Fuller
MRID No.: 49921708

Reviewer: Chris Jiang
Study Completion Date: April 26, 2016
Study No.: 19757-16

Testing Laboratory: Stillmeadow, Inc.
Author: Lori Carter

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Dosage: 0.1 mL

Species: One female and two male New Zealand White rabbits
Age: Twenty weeks
Weight: 2.7 to 3.0 kilograms at study start
Source: Veterinary Clinical Resources, Hutto, TX

Summary:

1. **Toxicity Category:** IV
2. **Classification:** Acceptable

Deviations from Guideline 870.2400: Relative humidity was at times outside protocol range. This deviation did not impact the integrity of the study.

Results:

Individual Scores for Ocular Irritation

Observations	Rabbit No. 01 (Female)				Rabbit No. 54 (Male)				Rabbit No. 26 (Male)			
	Hours After Treatment											
	1	24	48	72	1	24	48	72	1	24	48	72
I. Corneal Opacity	0	0	0	0	+	0	0	0	0	0	0	0
II. Iritis	0	0	0	0	0	0	0	0	0	0	0	0
III. Conjunctivae												
A. Redness	1	1	0	0	1	1	1	0	1	1	1	0
B. Chemosis	1	0	0	0	2	1	0	0	2	1	0	0
C. Discharge	0	0	0	0	2	0	0	0	1	0	0	0

+ - slight dulling of the luster
Both eyes were treated with fluorescein sodium ophthalmic solution, but staining did not occur in any eyes

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (870.2500)

Product Manager: Demson Fuller
MRID No.: 49921709

Reviewer: Chris Jiang
Study Completion Date: April 26, 2016
Study No.: 19758-16

Testing Laboratory: Stillmeadow, Inc.
Author: Lori Carter

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Dosage: 0.5 mL

Species: One male and two female New Zealand White rabbits
Age: Twelve weeks
Weight: 2.5 to 2.7 kilograms at study start
Source: Veterinary Clinical Resources, Hutto, TX

Summary:

1. **Toxicity Category:** IV
2. **Classification:** Acceptable

Deviations from Guideline 870.2400: Relative humidity was at times outside protocol range. First observation was at ¼ hour after unwrap. These deviations did not impact the integrity of the study.

Results:

Animal	Erythema / Edema Time After Patch Removal				
	1 hr	24 hrs	48 hrs	72 hrs	Day 7
0078-M	1/0	1/0	1/0	1/0	0/0
0067-F	0/0	0/0	0/0	0/0	0/0
0069-F	0/0	0/0	0/0	0/0	0/0

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (OCSPP 870.2600)

Product Manager: Demson Fuller
MRID No.: 49921710

Reviewer: Chris Jiang
Study Completion Date: May 9, 2016
Amended: May 16, 2016
Study No.: 19759-16

Testing Laboratory: Stillmeadow, Inc.
Author: Lori Carter

Quality Assurance (40 CFR §160): A statement of GLP compliance was included.

Test Material: CaviWipes Bleach, 16-1020RDO, clear solution
Positive Control: α-Hexylcinnamaldehyde (HCA)

Species: Hartley albino guinea pigs
Weight when tested: 356 to 488 grams
Age: Young adult
Source: Charles River Hdq. Wilmington, MA

Summary:

1. **This Product is not a dermal sensitizer.**
2. **Classification:** Acceptable

Procedure (Deviation From §81-6): No deviations occurred during the study

Procedure: After preliminary tests, the definitive study was undertaken. The Buehler method was tested for skin sensitization. Once each week for three weeks, either 0.4 mL or nothing was applied to the clipped left side of each animal. After the exposure period, the bindings were removed. The guinea pigs were scored at 24 and at 48 hours after each induction.
Two weeks after the final application, all animals were challenged with 0.4 mL of the test substance on the right side. The guinea pigs were scored at 24 and at 48 hours after challenge.

Results: At 24 hours no irritation after the first induction, at 48 hours after the first induction, at 24 hours after the second induction, at 48 hours after the second induction, at 24 hours after the third induction, and at 48 hours after the third induction, no irritation was observed.

At 24 hours after challenge and at 48 hours after challenge, no irritation was observed.

The historical positive control showed appropriate results.